Pharmacokinetics of Docetaxel in a Patient with Non-small Cell Lung Cancer Undergoing Continuous Ambulatory Peritoneal Dialysis

Hiroyasu Kaneda, MD, PhD, Isamu Okamoto, MD, PhD, and Kazuhiko Nakagawa, MD, PhD

CASE REPORT

There is no consensus and little information available regarding the suitability of administration of anticancer agents in patients with insufficient renal function who are undergoing treatment by continuous ambulatory peritoneal dialysis (CAPD) or hemodialysis. In CAPD, the dialysate is infused into the peritoneum through an indwelling catheter with the tip positioned in the pelvis, and the peritoneal membrane, a natural semipermeable membrane, serves as the dialyzer. CAPD is done at home, usually four or five times every day. Pharmacokinetic and pharmacodynamic analyses of anticancer agents in such patients are thus needed so that potential adverse events can be predicted and avoided. The cytotoxic drug docetaxel is metabolized by hepatic cytochrome P450 and is excreted through bile into feces.[1] Renal excretion of the drug is minimal (<5%). However, it is not known whether administration of docetaxel is safe in patients undergoing CAPD. We now present the first full pharmacokinetic analysis of docetaxel in a patient with non-small cell lung cancer (NSCLC) undergoing CAPD.

Case Presentation

A 76-year-old man with chronic renal failure attributed to diabetic nephropathy presented with a mass in the lower lobe of the left lung. Computed tomography (CT)-guided needle biopsy yielded a diagnosis of lung adenocarcinoma. Chest CT revealed a metastasis in the other lung and an enlarged hilar lymph node. The clinical stage of the patient was T2N1M1. Physical examination of the patient, who was undergoing CAPD, revealed no relevant findings, even though blood tests showed blood urea nitrogen and creatinine levels of 29.0 and 9.2 mg/dl, respectively. Other blood test parameters were within normal limits. The Eastern Cooperative Oncology Group performance status of the patient was 1.

The patient was treated with docetaxel at 60 mg/m^2 over 60 minutes on day 1 every 3 weeks, the standard recommended dose and scheduled in Japan. Diarrhea and febrile neutropenia of grade 3 developed during the first cycle but were manageable. Other adverse events included general fatigue, appetite loss, and anemia, which were also generally tolerable. Chest CT after two cycles of chemotherapy revealed stable disease for both the primary and metastatic lesions. However, subsequent chemotherapy was discontinued because of patient refusal.

Blood samples were collected before the first docetaxel infusion, 30 minutes after onset of the infusion, 5 minutes before the end of the infusion, as well as 0, 5, 10, 20, 30, 60, and 90 minutes and 2, 3, 4, 6, 8, 10, and 24 hours after infusion for pharmacokinetic analysis. The plasma concentration of docetaxel was measured by high-performance liquid chromatography.[2] The postinfusion plasma concentration of docetaxel showed a typical triphasic profile (Figure 1).[3] The area under the concentration-time curve and plasma clearance of docetaxel were 2.11 μg · h/ml and 25.1 L/h/m^2, respectively, consistent with values previously determined for patients with normal renal function (Table 1).[4]

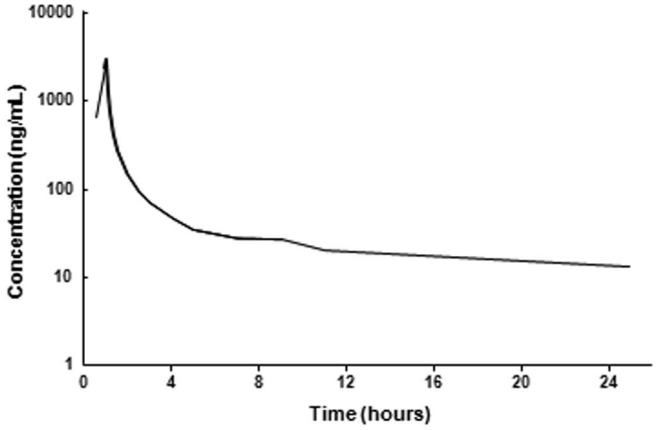

FIGURE 1. Plasma concentration versus time curve for the first cycle of docetaxel chemotherapy in the present case.

Department of Medical Oncology, Kinki University Faculty of Medicine, Osaka-Sayama, Osaka, Japan.
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Address for correspondence: Isamu Okamoto, MD, PhD, Department of Medical Oncology, Kinki University Faculty of Medicine, 377-2 Ohno-higashi, Osaka-Sayama, Osaka 589-8511, Japan. E-mail: chiokamoto@dotd.med.kindai.ac.jp

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TABLE 1. Pharmacokinetic Parameters for Docetaxel in the Present Case Compared with Those (Mean ± SD) Determined in a Previous Study of 30 Japanese Patients with Normal Renal Function[4]

Parameter	Present Case	Previous Study
C_{max} (μg/ml)	3.11	2.71 ± 0.4
$T_{1/2}$ (h)	15.5	9.2 ± 3.3
AUC (μg · h/ml)	2.11	2.71 ± 0.4
Clearance (L/h/m^2)	25.1	22.6 ± 3.4

DISCUSSION

Docetaxel is a key cytotoxic agent that shows marked activity against several cancers, including NSCLC. CAPD is an important renal replacement therapy for chronic renal failure patients. However, there is little information available and no consensus regarding the suitability of docetaxel administration in patients with insufficient renal function. We now report the first full pharmacokinetic analysis of docetaxel in a patient with NSCLC undergoing CAPD. The analysis revealed that CAPD appeared to have no effect on the pharmacokinetic parameters of docetaxel. The occurrence and severity of adverse events associated with docetaxel were also not increased as a result of the reduced renal function of the patient. Our data thus indicate that docetaxel administration was safe in the present patient and did not result in deterioration in his performance status. Pharmacokinetic and pharmacodynamic analyses of anticancer agents in patients with renal insufficiency will help to establish appropriate treatments that maximize efficacy while avoiding unacceptable toxicity. Further evaluation of the contribution of renal function to the efficacy and toxicity of docetaxel is warranted.

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